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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,838	HANSEN ET AL.	
	Examiner	Art Unit	
	Eric E. Silverman, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10-6-2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 – 37 are pending in this action.

Claim Objections

Claims 2 and 28 objected to because of the following informalities: claim 2 recites "a ionic agent" should be "an ionic agent". Claim 28 recites "hen", this seems to be a typographical error. It is believed that the claims should recite "when". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 7, 8, 10 – 12, 14 – 15, 17 – 19, and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

claims 1 – 7, 11, 12, and 16 – 19 of copending Application No. 10,602,340. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims differ from instant claims only in that instant independent claim 1 recites a minimum concentration of the salt, whereas copending independent claim 1 is silent on the concentration. However, copending claim 16 recites a range of concentrations for the salt, which substantially overlaps the concentration limitations of instant claim 1. Accordingly, it would be obvious to use the concentrations of more than 15 mM as recited in instant claim 1, since copending claim 16 teaches using concentrations in the range of 5 mM to 150 mM, and most of this range is labove 15 mM.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17, 27, and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. **This is a written description rejection**.

With regard to claim 17, the claim recites "methionine-containing peptide". There are a great number of methionine-containing peptides, and Applicant has not disclosed a sufficient number of species of this genus to show possession of the entire genus. Accordingly, a person of ordinary skill in the art would not recognize that Applicant was in possession of the entire genus of methionine-containing peptides, as claimed.

With regard to claims 27 and 28, the claims recite a factor VII sequence variant. There are an essentially infinite number of factor VII sequence variants, which include variants of any one peptide to variants where the entire peptide chain is varied from the original peptide to any other natural or synthetic peptide. Applicant has not disclosed a single example of factor VII sequence variant, as claimed. Accordingly, the artisan would certainly not recognize that Applicant was in possession of the entire genus of factor VII sequence variants.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for known sequence variants of factor VII proteins that show pharmaceutical efficacy, does not reasonably provide enablement for all factor VII sequence variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims recite a factor VII sequence variant.

State of the prior art: Variation of sequences in polypeptides is within the skill of the artisan. However, the skilled artisan would recognize that changing even member of a polypeptide sequence can vastly alter the reactivity and function of the polypeptide. The artisan would know that even small alterations may cause a polypeptide to not function in its typical manner, or may alter its function.

Existence of working examples/specification: The specification does not disclose any example of a factor VII sequence variant.

Amount of experimentation necessary: In order to use the claimed composition for its disclosed use, namely as a pharmaceutical one of ordinary skill in the art would have to first obtain the entire, essentially infinite number of sequence variants of factor VII, screen the same for pharmaceutical efficacy, find optimal conditions for formulation of same, and test same for both function and adverse effects in animals and humans.

It would require undo experimentation for one of skill in the art to practice the claimed invention. Therefore, the claimed invention of a composition of factor VII sequence variants is not fully enabled by instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 11, 13, 17, 21, 23, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 11, 21, and 32 recite improper Markush groups.

Claim 11 recites "a small peptide". The specification does not define what is meant by the relative word "small", and as such, a person of ordinary skill in the art would not understand the metes and bounds of the claimed invention.

Claim 13 recites "where the concentration is". It is unclear what component is being referred to in this recitation.

Claim 17 recites "methionine-analogue" and "methionine-homologue". The artisan would not know what compounds are included by these terms, and accordingly, a person of ordinary skill in the art would not be able to interpret the metes and bounds of the claimed invention.

Claim 23 recites the limitation "the buffer" in claim 22. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 3, 5 – 7,10 – 12, 20 – 22, 29 – 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Hannam et al, US 5,649,959.

Hannam discloses a fibrin sealant kit for use in clinical trials, wherein the kit contains factor VII, Tris buffer at a pH of 7.5, and calcium chloride in amounts commensurate with instant claims (col. 9, lines 10 – 21).

With regard to claim 25, the stability of the composition is a property of its components, accordingly, since the prior art composition has the same components as the composition of this claim, the stability will be the same.

Claims 1 – 7, 9 – 16, 20 - 23, 25, 26 and 29 – 37, are rejected under 35 U.S.C. 102(b) as being anticipated by The Medicine Catalogue (Laegemiddel Kataloget), of record. Note that the date of public availability of this reference has been determined to be July 19, 2000, thus qualifying the reference as prior art under 102(b).

The Medicine Catalog discloses a composition with recombinant coagulation factor VIIa, with 105 mg calcium chloride, 1.3 mg glycylglycine, 30 mg mannitol, 3.0 mg sodium chloride and 0.1 mg polysorbate 80 per mL, wherein the composition has a pH of 5.4 – 6.0.

With regard to claim 25, the stability of the composition is a property of its components, accordingly, since the prior art composition has the same components as the composition of this claim, the stability will be the same.

With regard to claim 29, the amount of water used is disclosed (see uner the heading "preparation of injection fluid", and a simple calculation reveals that the concentration of the factor VII is 0.6 mg/mL.

The Medicine Catalog also teaches that the preparations are dissolved in varying amounts of sterile water, and that they are administered by a bolus injection (see under the heading "suggested dosage").

The concentrations recited in instant claims are not explicitly disclosed. However since different amounts of sterile water are used to reconstitute the composition of the prior art while the mass of the excipients does not change, it is deemed inherent that the concentration of the excipients in at least one embodiment of the prior art (that is, with either 2 mL, 4 mL or 8 mL of sterile water used to reconstitute the composition of the prior art) the concentrations of the excipients will be commensurate with instant claims.

In addition, since in the process of reconstituting the dry powder, water is added over a short, albeit finite, period of time, at some point during the addition of the water the concentration of the solutes of the prior art would be commensurate with that of instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 6, 12, 13, 22, 23, 30, 31 – 37 are rejected under 35 U.S.C. 103(a) as unpatentable over The Medicine Catalogue (Laegemiddel Kataloget), of record.

The teachings of The Medicine Catalog are discussed above.

The amount concentrations of materials are not explicitly disclosed, although they are believed to be implicit, vide supra.

If the concentrations are different from that of instant claims, it would certainly be obvious to a person of ordinary skill in the art to vary the concentrations of the excipients, with the motivation being to obtain the best possible result. The artisan would enjoy a reasonable expectation of success since the prior art teaches varying these concentrations by reconstituting the same mass of excipients with different amounts of sterile water.

Claims 8, is rejected under 35 U.S.C. 103(a) as being unpatentable over The Medical Catalog (Laegemiddel Kataloget), of record, in combination with WO 97/19687, of record.

The teachings of The Medical Catalog are discussed above.

WO 97/19687 teaches that calcium, magnesium and manganese are equivalent divalent metal ions in the art of protein stabilization (page 27).

As such, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to substitute magnesium for calcium in the teachings of The Medical Catalog, with the motivation being that the two are equivalents in the art. The expected result would be a composition that had magnesium chloride instead of calcium chloride. Since the calcium and magnesium are art recognized equivalents, the artisan would enjoy a reasonable expectation of success.

Claims 17 – 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medical Catalog (Laegemiddel Kataloget), of record as applied to claims 5, 6, 12, 13, 22, 23, 30, 31 – 37 above, and further in view of Thatcher et al., US 5,830,852.

The teachings of The Medical Journal are discussed above.

The Medical Journal does not teach methionine.

Thatcher teaches the use of methionine as an anti-oxidant in peptide containing compositions (Example III). Thatcher further teaches using amounts commensurate with the scope of instant claims.

Accordingly, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to add methionine to the composition of The Medical Journal. The motivation to do so comes from Thatcher, who teaches the utility of methinine as an anti-oxidant in peptide compositions. The artisan would thus expect the

resulting composition to be protected against oxidation. Since Thatcher teaches the utility of this agent, the artisan would also enjoy a reasonable expectation of success.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Medical Catalog (Laegemiddel Kataloget), of record as applied to claims 5, 6, 12, 13, 22, 23, 30, 31 – 37 above, and further in view of Osawa et al., US 5,993,795.

The teachings of The Medical Journal are discussed above.

The Medical Journal does not teach the use of the compounds of claim 24.

Osawa teaches the use of methyl and propyl paraben as preservatives in compositions containing proteins (example 13).

Accordingly, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to use methyl or propyl paraben in the composition of The Medical Journal. The motivation to do so comes from Osawa, who teaches the utility of such compounds in protein compositions. The expected result would be a more stable composition. Since Oswa teaches the utility of parabens, the artisan would have a reasonable expectation of success.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is 571 272 5549. The examiner can normally be reached on Monday to Friday 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571 272 0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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